

PATENT APPLICATION

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant : Conklin, Darrell C., and Blumberg, Hal

Application No. :

Filed :

For : A HUMAN 2-19 PROTEIN HOMOLOGUE, Z219A

Examiner :

Art Unit :

Docket No. : 97-63C1

Date : October 26, 2001

Box Non-Fee Amendment

Assistant Commissioner for Patents

Washington, D.C. 20231

**PRELIMINARY AMENDMENT**

Dear Sir:

Applicant respectfully requests consideration of the following preliminary amendments. Please amend the subject application as follows:

IN THE CLAIMS

Please cancel claims 1-21 without prejudice to the prosecution thereof in a subsequent application.

Please add the following new claims:

-22. An isolated polynucleotide that hybridizes to the 21q22.3 region of human chromosome 21 under hybridization wash conditions of 0.1XSSC to 2XSSC, 0.1% SDS at 55°C-65°C and that encodes a polypeptide comprising a sequence of amino acid residues that is at least 90% identical to an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr), to amino acid number 235 (Ser); and

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 235 (Ser); and

(c) polynucleotide molecules complementary to (a) or (b).

23. An isolated polynucleotide according to claim 22, wherein the polynucleotide encodes a polypeptide comprising a sequence of amino acid residues that is at least 95% identical to an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr), to amino acid number 235 (Ser); and

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 235 (Ser); and

(c) polynucleotide molecules complementary to (a) or (b).

24. An isolated polynucleotide according to claim 22, wherein the polynucleotide encodes a polypeptide comprising a sequence of amino acid residues comprising an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr), to amino acid number 235 (Ser); and

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 235 (Ser); and

(c) polynucleotide molecules complementary to (a) or (b).

25. An isolated polynucleotide according to claim 24, wherein the polynucleotide encodes a polypeptide that consists of a sequence of amino acid residues as shown in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser); or amino acid 1 (Met), to amino acid number 235 (Ser).

26. The isolated polynucleotide molecule of claim 22, wherein the polynucleotide encodes a polypeptide that further contains motifs 1, 2, 3, 4 and 5 spaced apart from N-terminus to C-terminus in a configuration M1-{25-26}-M2-{15}-M3-{11}-M4-{34-36}-M5,

wherein M1 is “motif 1,” a sequence of amino acids as shown in amino acids 127 to 129 of SEQ ID NO:2,

M2 is “motif 2,” a sequence of amino acids as shown in amino acids 156 to 158 of SEQ ID NO:2,

M3 is “motif 3,” a sequence of amino acids as shown in amino acids 174 to 176 of SEQ ID NO:2,

M4 is “motif 4,” a sequence of amino acids as shown in amino acids 188 to 190 of SEQ ID NO:2, and

M5 is “motif 5,” a sequence of amino acids as shown in amino acids 227 to 229 of SEQ ID NO:2), and

{#} denotes the number of amino acids between the motifs.

27. A vector comprising the following operably linked elements:  
a transcription promoter;  
a DNA segment that hybridizes to the 21q22.3 region of human chromosome 21 under hybridization wash conditions of 0.1XSSC to 2XSSC, 0.1% SDS at 55°C-65°C and that encodes a polypeptide comprising an amino acid sequence as shown in SEQ ID NO:2 from

amino acid number 26 (Tyr) to amino acid number 235 (Ser); or 1 (Met) to amino acid number 235 (Ser); and

a transcription terminator,

wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.

28. A vector according to claim 27, wherein the vector is an expression vector.

29. A cell into which has been introduced a vector according to claim 27.

30. An expression vector comprising the following operably linked elements:

a transcription promoter;

a DNA segment comprising a polynucleotide selected from the group consisting of:

(a) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 194 to nucleotide 823;

(b) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 119 to nucleotide 823;

(c) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 1 to nucleotide 705;

(d) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 76 to nucleotide 705; and

(e) polynucleotide molecules complementary to (a), (b), (c) or (d); and

a transcription terminator,

wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.

31. A cell into which has been introduced a vector according to claim 30.

32. An isolated polypeptide comprising a sequence of amino acid residues selected from the group consisting of:

(a) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser) of SEQ ID NO:2; and

(b) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid residue number 1 (Met) to amino acid residue number 235 (Ser).

33. An isolated polypeptide according to claim 32, wherein the polypeptide consists of a sequence of amino acid residues selected from the group consisting of:

(a) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser) of SEQ ID NO:2; and

(b) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid residue number 1 (Met) to amino acid residue number 235 (Ser).

34. A method of producing a polypeptide comprising:

culturing a cell according to claim 31; and

isolating the polypeptide produced by the cell.

35. A method of producing an antibody to a polypeptide comprising:

inoculating an animal with a polypeptide selected from the group consisting of:

(a) a polypeptide consisting of 9 to 210 amino acids, wherein the polypeptide comprises a contiguous sequence of amino acids in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser);

(b) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser);

(c) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid number 59 (Arg) to amino acid number 133 (Asp);

(d) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid number 135 (Ser) to amino acid number 212 (Ala);

(e) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid 215 (Asn) to amino acid number 231 (Pro); and

wherein the polypeptide elicits an immune response in the animal to produce the antibody; and

isolating the antibody from the animal.

36. An antibody produced by the method of claim 35, which specifically binds to a polypeptide of SEQ ID NO:2.

37. An antibody that specifically binds to a polypeptide of claim 32.

38. A method of detecting, in a test sample, the presence of an antagonist of z219a protein activity, comprising:

transfected a z219a-responsive cell, with a reporter gene construct that is responsive to a z219a-stimulated cellular pathway; and

producing a z219a polypeptide by the method of claim 34; and

adding the z219a polypeptide to the cell, in the presence and absence of a test sample; and

comparing levels of response to the z219a polypeptide, in the presence and absence of the test sample, by a biological or biochemical assay; and

determining from the comparison, the presence of the antagonist of z219a activity in the test sample.

39. A method of detecting, in a test sample, the presence of an agonist of z219a protein activity, comprising:

transfected a z219a-responsive cell, with a reporter gene construct that is responsive to a z219a-stimulated cellular pathway; and

adding a test sample; and

comparing levels of response in the presence and absence of the test sample, by a biological or biochemical assay; and

determining from the comparison, the presence of the agonist of z219a activity in the test sample.

40. A method for detecting a chromosome 21 trisomy or partial trisomy in a patient sample, comprising:

(i) obtaining a genetic sample from a patient;

(ii) hybridizing the genetic sample with a polynucleotide comprising a nucleotide sequence selected from the group consisting of:

(a) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 194 to nucleotide 823;

(b) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 119 to nucleotide 823;

(c) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 1 to nucleotide 705;

(d) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 76 to nucleotide 705; and

(c) polynucleotide molecules complementary to (a), (b), (c) or (d); and,

wherein hybridization conditions comprise 0.1XSSC to 2XSSC, 0.1% SDS at 55°C-65°C, wherein the genetic sample and the polynucleotide will hybridize and hence create a hybridization product,

(iii) visualizing the hybridization product; and

(iv) comparing the hybridization product to a control reaction product,

wherein the control reaction product is produced from a control genetic sample from a control patient without chromosome 21 trisomy or partial trisomy using the method of (i)-(iv), and

wherein a difference between said hybridization product and said control reaction product is indicative of chromosome 21 trisomy or partial trisomy in the patient.--

**REMARKS**

Claims 1-21, filed with the original case, are pending in the instant continuation application. In favor of a new claim set concerning different embodiments of the invention, claims 1-21 were canceled without prejudice to the prosecution thereof in a subsequent application. Newly added claims 22-40 were added as replacement claims. Support for the newly added claims are provided throughout the specification, and the original claim set; and particularly at page 20, lines 26-31; original claim 2; SEQ ID NO:1; SEQ ID NO:8; page 14, lines 1-9; page 15, lines 23-26; page 15, line 35, to page 16, line 13; page 72, line 13, to page 74, line 12; and Example 3. A marked-up version of the changes made to claims by the current amendment, "Explanation Of Amendments With Markings," is provided. An Appendix with the claim set including the new claims is provided for the Examiner's convenience, and shall not be construed as submission of a re-presented claim set under 37 CFR §1.121. No new matter was added by these amendments.

Early reconsideration and allowance of the pending claims is respectfully requested. If the Patent Examiner believes that a telephone interview would expedite prosecution of this patent application, please call the undersigned at (206) 442-6676.

Respectfully Submitted,

Darrell C. Conklin et al.



Jennifer K. Johnson, J.D.

Registration No. 43,696

Enclosures:

Amendment Fee Transmittal (in duplicate)

Explanation of Amendments with Markings (11 pages)

Appendix (6 pages)

Postcard

**EXPLANATION OF AMENDMENTS WITH MARKINGS TO SHOW CHANGES  
MADE**

Please cancel claims 1-21 without prejudice to the prosecution thereof in a subsequent application:

1. An isolated polynucleotide that encodes a polypeptide comprising a sequence of amino acid residues that is at least 90% identical to an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr), to amino acid number 235 (Ser), and

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 235 (Ser).

2. An isolated polynucleotide molecule selected from the group consisting of:

(a) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 194 to nucleotide 823;

(b) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 119 to nucleotide 823; and

(c) polynucleotide molecules complementary to (a) or (b).

3. An isolated polynucleotide sequence according to claim 1, wherein the polynucleotide comprises nucleotide 1 to nucleotide 705 of SEQ ID NO:8.

4. An isolated polynucleotide according to claim 1, wherein the polypeptide consists of a sequence of amino acid residues that is at least 90% identical to an amino acid sequence

as shown in SEQ ID NO:2 from amino acid number 26 (Tyr), to amino acid number 235 (Ser).

5. An isolated polynucleotide according to claim 4, wherein the z219a polypeptide consists of a sequence of amino acid residues as shown in SEQ ID NO:2 from amino acid number 26 (Tyr), to amino acid number 235 (Ser).

6. The isolated polynucleotide molecule of claim 1, wherein the polynucleotide encodes a polypeptide that contains motifs 1, 2, 3, 4 and 5 spaced apart from N terminus to C terminus in a configuration M1 {25-26} M2 {15} M3 {11} M4 {34-36} M5.

7. An expression vector comprising the following operably linked elements:

a transcription promoter;

a DNA segment encoding a z219a polypeptide that is at least 90% identical to an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr), to amino acid number 235 (Ser); and

a transcription terminator,

wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.

8. An expression vector according to claim 7, further comprising a secretory signal sequence operably linked to the DNA segment.

9. A cultured cell into which has been introduced an expression vector according to claim 7, wherein the cell expresses the polypeptide encoded by the DNA segment.

10. A DNA construct encoding a fusion protein, the DNA construct comprising:

a first DNA segment encoding a polypeptide that is at least 90% identical to a sequence of amino acid residues 1 (Met) through 25 (Gly) of SEQ ID NO:2, and

second DNA segment encoding an additional polypeptide, wherein the first and second DNA segments are connected in frame; and

encode the fusion protein.

11. An isolated polypeptide comprising a sequence of amino acid residues that is at least 90% identical to an amino acid sequence selected from the group consisting of:

(a) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser) of SEQ ID NO:2, and

(b) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid residue number 1 (Met) to amino acid residue number 235 (Ser).

12. An isolated polypeptide according to claim 11, wherein the polypeptide consists of a sequence of amino acid residues that is at least 90% identical to an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser).

13. An isolated polypeptide according to claim 12, wherein the sequence of amino acid residues is as shown in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser).

14. The isolated polypeptide of claim 11, wherein the polypeptide molecule encodes motifs 1, 2, 3, 4 and 5 spaced apart from N terminus to C terminus in a configuration M1 {25-26} M2 {15} M3 {11} M4 {34-36} M5.

15. A method of producing a z219a polypeptide comprising:

culturing a cell according to claim 9; and  
isolating the z219a polypeptide produced by the cell.

16. A method of producing an antibody to z219a polypeptide comprising:

inoculating an animal with a polypeptide selected from the group consisting of:

(a) a polypeptide consisting of 9 to 210 amino acids, wherein the polypeptide is at least 90% identical to a contiguous sequence of amino acids in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser);

(b) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser);

(c) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid number 59 (Arg) to amino acid number 133 (Asp);

(d) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid number 135 (Ser) to amino acid number 212 (Ala);

(e) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid 215 (Asn) to amino acid number 231 (Pro); and

wherein the polypeptide elicits an immune response in the animal to produce the antibody; and

isolating the antibody from the animal.

17. An antibody produced by the method of claim 16, which specifically binds to a z219a polypeptide.

18. The antibody of claim 17, wherein the antibody is a monoclonal antibody.

19. An antibody which specifically binds to a polypeptide of claim 11.

20. A method of detecting, in a test sample, the presence of an antagonist of z219a protein activity, comprising:

transfecting a z219a responsive cell, with a reporter gene construct that is responsive to a z219a stimulated cellular pathway; and

producing a z219a polypeptide by the method of claim 15; and

adding the z219a polypeptide to the cell, in the presence and absence of a test sample; and

comparing levels of response to the z219a polypeptide, in the presence and absence of the test sample, by a biological or biochemical assay; and

determining from the comparison, the presence of the antagonist of z219a activity in the test sample.

21. A method of detecting, in a test sample, the presence of an agonist of z219a protein activity, comprising:

transfecting a z219a responsive cell, with a reporter gene construct that is responsive to a z219a stimulated cellular pathway; and

adding a test sample; and

~~comparing levels of response in the presence and absence of the test sample, by a biological or biochemical assay, and~~

~~determining from the comparison, the presence of the agonist of z219a activity in the test sample.~~

Please add the following new claims:

--22. An isolated polynucleotide that hybridizes to the 21q22.3 region of human chromosome 21 under hybridization wash conditions of 0.1XSSC to 2XSSC, 0.1% SDS at 55°C-65°C and that encodes a polypeptide comprising a sequence of amino acid residues that is at least 90% identical to an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr), to amino acid number 235 (Ser); and
- (b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 235 (Ser); and
- (c) polynucleotide molecules complementary to (a) or (b).

23. An isolated polynucleotide according to claim 22, wherein the polynucleotide encodes a polypeptide comprising a sequence of amino acid residues that is at least 95% identical to an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr), to amino acid number 235 (Ser); and
- (b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 235 (Ser); and
- (c) polynucleotide molecules complementary to (a) or (b).

24. An isolated polynucleotide according to claim 22, wherein the polynucleotide encodes a polypeptide comprising a sequence of amino acid residues comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr), to amino acid number 235 (Ser); and

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 235 (Ser); and

(c) polynucleotide molecules complementary to (a) or (b).

25. An isolated polynucleotide according to claim 24, wherein the polynucleotide encodes a polypeptide that consists of a sequence of amino acid residues as shown in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser); or amino acid 1 (Met), to amino acid number 235 (Ser).

26. The isolated polynucleotide molecule of claim 22, wherein the polynucleotide encodes a polypeptide that further contains motifs 1, 2, 3, 4 and 5 spaced apart from N-terminus to C-terminus in a configuration M1-{25-26}-M2-{15}-M3-{11}-M4-{34-36}-M5,

wherein M1 is "motif 1," a sequence of amino acids as shown in amino acids 127 to 129 of SEQ ID NO:2,

M2 is "motif 2," a sequence of amino acids as shown in amino acids 156 to 158 of SEQ ID NO:2,

M3 is "motif 3," a sequence of amino acids as shown in amino acids 174 to 176 of SEQ ID NO:2,

M4 is "motif 4," a sequence of amino acids as shown in amino acids 188 to 190 of SEQ ID NO:2, and

M5 is "motif 5," a sequence of amino acids as shown in amino acids 227 to 229 of SEQ ID NO:2), and

{#} denotes the number of amino acids between the motifs.

27. A vector comprising the following operably linked elements:  
a transcription promoter;  
a DNA segment that hybridizes to the 21q22.3 region of human chromosome 21 under hybridization wash conditions of 0.1XSSC to 2XSSC, 0.1% SDS at 55°C-65°C and that encodes a polypeptide comprising an amino acid sequence as shown in SEQ ID NO:2 from

amino acid number 26 (Tyr) to amino acid number 235 (Ser); or 1 (Met) to amino acid number 235 (Ser); and

a transcription terminator,

wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.

28. A vector according to claim 27, wherein the vector is an expression vector.

29. A cell into which has been introduced a vector according to claim 27.

30. An expression vector comprising the following operably linked elements:

a transcription promoter;

a DNA segment comprising a polynucleotide selected from the group consisting of:

(a) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 194 to nucleotide 823;

(b) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 119 to nucleotide 823;

(c) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 1 to nucleotide 705;

(d) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 76 to nucleotide 705; and

(e) polynucleotide molecules complementary to (a), (b), (c) or (d); and

a transcription terminator,

wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.

31. A cell into which has been introduced a vector according to claim 30.

32. An isolated polypeptide comprising a sequence of amino acid residues selected from the group consisting of:

(a) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser) of SEQ ID NO:2; and

(b) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid residue number 1 (Met) to amino acid residue number 235 (Ser).

33. An isolated polypeptide according to claim 32, wherein the polypeptide consists of a sequence of amino acid residues selected from the group consisting of:

(a) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser) of SEQ ID NO:2; and

(b) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid residue number 1 (Met) to amino acid residue number 235 (Ser).

34. A method of producing a polypeptide comprising:

culturing a cell according to claim 31; and

isolating the polypeptide produced by the cell.

35. A method of producing an antibody to a polypeptide comprising:

inoculating an animal with a polypeptide selected from the group consisting of:

(a) a polypeptide consisting of 9 to 210 amino acids, wherein the polypeptide comprises a contiguous sequence of amino acids in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser);

(b) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser);

(c) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid number 59 (Arg) to amino acid number 133 (Asp);

(d) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid number 135 (Ser) to amino acid number 212 (Ala);

(e) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid 215 (Asn) to amino acid number 231 (Pro); and

wherein the polypeptide elicits an immune response in the animal to produce the antibody; and

isolating the antibody from the animal.

36. An antibody produced by the method of claim 35, which specifically binds to a polypeptide of SEQ ID NO:2.

37. An antibody that specifically binds to a polypeptide of claim 32.

38. A method of detecting, in a test sample, the presence of an antagonist of z219a protein activity, comprising:

transfected a z219a-responsive cell, with a reporter gene construct that is responsive to a z219a-stimulated cellular pathway; and

producing a z219a polypeptide by the method of claim 34; and

adding the z219a polypeptide to the cell, in the presence and absence of a test sample; and

comparing levels of response to the z219a polypeptide, in the presence and absence of the test sample, by a biological or biochemical assay; and

determining from the comparison, the presence of the antagonist of z219a activity in the test sample.

39. A method of detecting, in a test sample, the presence of an agonist of z219a protein activity, comprising:

transfected a z219a-responsive cell, with a reporter gene construct that is responsive to a z219a-stimulated cellular pathway; and

adding a test sample; and

comparing levels of response in the presence and absence of the test sample, by a biological or biochemical assay; and

determining from the comparison, the presence of the agonist of z219a activity in the test sample.

40. A method for detecting a chromosome 21 trisomy or partial trisomy in a patient sample, comprising:

(i) obtaining a genetic sample from a patient;

(ii) hybridizing the genetic sample with a polynucleotide comprising a nucleotide sequence selected from the group consisting of:

(a) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 194 to nucleotide 823;

(b) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 119 to nucleotide 823;

(c) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 1 to nucleotide 705;

(d) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 76 to nucleotide 705; and

(c) polynucleotide molecules complementary to (a), (b), (c) or (d); and,

wherein hybridization conditions comprise 0.1XSSC to 2XSSC, 0.1% SDS at 55°C-65°C, wherein the genetic sample and the polynucleotide will hybridize and hence create a hybridization product,

(iii) visualizing the hybridization product; and

(iv) comparing the hybridization product to a control reaction product,

wherein the control reaction product is produced from a control genetic sample from a control patient without chromosome 21 trisomy or partial trisomy using the method of (i)-(iv), and

wherein a difference between said hybridization product and said control reaction product is indicative of chromosome 21 trisomy or partial trisomy in the patient.--

**APPENDIX****Claim Set with Added Claims****WHAT IS CLAIMED IS:**

22. An isolated polynucleotide that hybridizes to the 21q22.3 region of human chromosome 21 under hybridization wash conditions of 0.1XSSC to 2XSSC, 0.1% SDS at 55°C-65°C and that encodes a polypeptide comprising a sequence of amino acid residues that is at least 90% identical to an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr), to amino acid number 235 (Ser); and
- (b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 235 (Ser); and
- (c) polynucleotide molecules complementary to (a) or (b).

23. An isolated polynucleotide according to claim 22, wherein the polynucleotide encodes a polypeptide comprising a sequence of amino acid residues that is at least 95% identical to an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr), to amino acid number 235 (Ser); and
- (b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 235 (Ser); and
- (c) polynucleotide molecules complementary to (a) or (b).

24. An isolated polynucleotide according to claim 22, wherein the polynucleotide encodes a polypeptide comprising a sequence of amino acid residues comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr), to amino acid number 235 (Ser); and
- (b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 235 (Ser); and

(c) polynucleotide molecules complementary to (a) or (b).

25. An isolated polynucleotide according to claim 24, wherein the polynucleotide encodes a polypeptide that consists of a sequence of amino acid residues as shown in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser); or amino acid 1 (Met), to amino acid number 235 (Ser).

26. The isolated polynucleotide molecule of claim 22, wherein the polynucleotide encodes a polypeptide that further contains motifs 1, 2, 3, 4 and 5 spaced apart from N-terminus to C-terminus in a configuration M1-{25-26}-M2-{15}-M3-{11}-M4-{34-36}-M5,

wherein M1 is "motif 1," a sequence of amino acids as shown in amino acids 127 to 129 of SEQ ID NO:2,

M2 is "motif 2," a sequence of amino acids as shown in amino acids 156 to 158 of SEQ ID NO:2,

M3 is "motif 3," a sequence of amino acids as shown in amino acids 174 to 176 of SEQ ID NO:2,

M4 is "motif 4," a sequence of amino acids as shown in amino acids 188 to 190 of SEQ ID NO:2, and

M5 is "motif 5," a sequence of amino acids as shown in amino acids 227 to 229 of SEQ ID NO:2), and

{#} denotes the number of amino acids between the motifs.

27. A vector comprising the following operably linked elements:

a transcription promoter;

a DNA segment that hybridizes to the 21q22.3 region of human chromosome 21 under hybridization wash conditions of 0.1XSSC to 2XSSC, 0.1% SDS at 55°C-65°C and that encodes a polypeptide comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser); or 1 (Met) to amino acid number 235 (Ser); and

a transcription terminator,  
wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.

28. A vector according to claim 27, wherein the vector is an expression vector.

29. A cell into which has been introduced a vector according to claim 27.

30. An expression vector comprising the following operably linked elements:  
a transcription promoter;  
a DNA segment comprising a polynucleotide selected from the group consisting of:

(a) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 194 to nucleotide 823;

(b) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 119 to nucleotide 823;

(c) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 1 to nucleotide 705;

(d) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 76 to nucleotide 705; and

(e) polynucleotide molecules complementary to (a), (b), (c) or (d); and  
a transcription terminator,

wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.

31. A cell into which has been introduced a vector according to claim 30.

32. An isolated polypeptide comprising a sequence of amino acid residues selected from the group consisting of:

(a) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser) of SEQ ID NO:2; and

(b) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid residue number 1 (Met) to amino acid residue number 235 (Ser).

33. An isolated polypeptide according to claim 32, wherein the polypeptide consists of a sequence of amino acid residues selected from the group consisting of:

(a) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser) of SEQ ID NO:2; and

(b) polypeptide molecules comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid residue number 1 (Met) to amino acid residue number 235 (Ser).

34. A method of producing a polypeptide comprising:  
culturing a cell according to claim 31; and  
isolating the polypeptide produced by the cell.

35. A method of producing an antibody to a polypeptide comprising:  
inoculating an animal with a polypeptide selected from the group consisting of:

(a) a polypeptide consisting of 9 to 210 amino acids, wherein the polypeptide comprises a contiguous sequence of amino acids in SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser);

(b) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid number 26 (Tyr) to amino acid number 235 (Ser);

(c) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid number 59 (Arg) to amino acid number 133 (Asp);

(d) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid number 135 (Ser) to amino acid number 212 (Ala);

(e) a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 from amino acid 215 (Asn) to amino acid number 231 (Pro); and  
wherein the polypeptide elicits an immune response in the animal to produce the antibody; and  
isolating the antibody from the animal.

36. An antibody produced by the method of claim 35, which specifically binds to a polypeptide of SEQ ID NO:2.

37. An antibody that specifically binds to a polypeptide of claim 32.

38. A method of detecting, in a test sample, the presence of an antagonist of z219a protein activity, comprising:

transfected a z219a-responsive cell, with a reporter gene construct that is responsive to a z219a-stimulated cellular pathway; and

producing a z219a polypeptide by the method of claim 34; and

adding the z219a polypeptide to the cell, in the presence and absence of a test sample; and

comparing levels of response to the z219a polypeptide, in the presence and absence of the test sample, by a biological or biochemical assay; and

determining from the comparison, the presence of the antagonist of z219a activity in the test sample.

39. A method of detecting, in a test sample, the presence of an agonist of z219a protein activity, comprising:

transfected a z219a-responsive cell, with a reporter gene construct that is responsive to a z219a-stimulated cellular pathway; and

adding a test sample; and

comparing levels of response in the presence and absence of the test sample, by a biological or biochemical assay; and

determining from the comparison, the presence of the agonist of z219a activity in the test sample.

40. A method for detecting a chromosome 21 trisomy or partial trisomy in a patient sample, comprising:

(i) obtaining a genetic sample from a patient;

(ii) hybridizing the genetic sample with a polynucleotide comprising a nucleotide sequence selected from the group consisting of:

(a) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 194 to nucleotide 823;

(b) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 119 to nucleotide 823;

(c) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 1 to nucleotide 705;

(d) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 76 to nucleotide 705; and

(c) polynucleotide molecules complementary to (a), (b), (c) or (d); and,

wherein hybridization conditions comprise 0.1XSSC to 2XSSC, 0.1% SDS at 55°C-65°C, wherein the genetic sample and the polynucleotide will hybridize and hence create a hybridization product,

(iii) visualizing the hybridization product; and

(iv) comparing the hybridization product to a control reaction product,

wherein the control reaction product is produced from a control genetic sample from a control patient without chromosome 21 trisomy or partial trisomy using the method of (i)-(iv), and

wherein a difference between said hybridization product and said control reaction product is indicative of chromosome 21 trisomy or partial trisomy in the patient.